think we all need to know where those numbers came from.

DR. FEARNOT: That is a good question. I can answer part of it, and you can answer.

The database of MAUDE or MDR reported events is an FDA database, and anybody who is a manufacturer that supplies a device, when they receive information from a physician or health care provider of any type that their device was involved in some event, adverse event, then takes that event and decides whether or not it meets the criteria for Federal submission.

So there are guidelines for when these devices need to be reported to FDA, and manufacturers then report those events to the Federal database. The database is accessible to anyone to look at these. That's why I could get access to them, but it is a Federal database, and it is required by law that reporting be made.

So manufacturers are submitting that information that they receive to the Federal database. I can tell you that not all of -- In fact, it's

usually a small portion of the reported events actually have to do with a specific device.

As a safe and sort of legally conservative approach, if we are notified that there was a problem with a patient and our device as well as ten other devices were being used in that procedure, we will submit it anyway, even though it may or may not have a direct -- the complication may or may not have a direct relationship to our device.

So in that sense, many of those may be over-reported. In another sense, there are likely to be procedures where the notification doesn't occur. So it is under-reported.

So in the balance, all I can say is that, as caregivers give information to manufacturers about procedures where there is an adverse event and their devices were involved, those reports are entered into that Federal database.

It does give a snapshot of the types of problems that may be associated with a procedure, and in this case balloon ruptures are in there all the way through deaths.

I don't know if that helps.

DR. HARTZ: You gave us a figure that the malfunction rate has decreased from 80 percent to 66 percent. Of what? What's the denominator? Like I said, the death figures and injury figures you give are similar to the meta analyses. What is that a percent of? It's extraordinarily high. So it can't refer to all angioplasties. What number does it refer to?

DR. FEARNOT: It refers to the total reported events.

DR. HARTZ: To only adverse events?

DR. FEARNOT: Just adverse. Of the adverse events, that's how many were in each of those categories. The actual proportion of adverse events to total angioplasties is very low, but what we took was all reported MDR and MAUDE events and then broke it into categories.

So you can see certain types of complications changing between the MDR and the MAUDE databases.

MR. DILLARD: Jim Dillard. I will maybe

provide a couple of thoughts also, which is it is very difficult to take the MAUDE and/or MDR database information and try to apply numerator and/or denominator sorts of interpretations with those databases.

I think we generally try to use them, certainly, for trends. They are good for trends, if we see things slowly increasing or decreasing over time, as well as very one-time or spike kinds of rates where we see a dramatic change over a very short period of time.

It generally gives us some information to go look at a particular place or in a particular location to see if there isn't something happening either with a specific type of device or over a total product category.

So I would hesitate to try to say that we can do any real number crunching on the MAUDE or the MDR data information, and I would use it more as qualitative kinds of information at this point.

DR. HARTZ: My other comments mostly concern the top slide on that page, again on page 8,

potential benefits.

Are you concerned that downclassifying this device may lead to unnecessary angioplasty? In other words, I gave the numbers. Is this going to lead to angioplasty when medical therapy would be perfectly adequate?

I am asking that question specifically because you stated that this procedure may be less traumatic and a less expensive alternative to bypass surgery, but you have not stated it in reference to medical therapy.

In addition, you have a section in another slide that said under special controls in order to avoid restenosis crossover to stent, and that gets to your point that most of these patients are going to end up with stents.

So I don't think -- I am concerned about the statement that it may be less traumatic and less expensive, but I am more concerned that the patient with less disease is likely to be treated. I'm not sure that's appropriate in today's environment, and I want to know what your thoughts are. I think we all

probably want to know what your thoughts are.

DR. FEARNOT: That's a real interesting question. I think, to answer that question, we have to look at motivation. I don't see the motivation at this point in today's environment for doing more angioplasty procedures on patients with lower -- with less disease unless it is medically motivated.

I can't see how the regulatory process for approval actually would affect that decision. I mean, it is really a resource decision for FDA and a resource decision for companies.

I mean, the only possible effect I can see would be that, if the cost of the products went down slightly, it might have some impact on that. But I think the question you are answering really is independent of the regulatory process.

Now they may be used for patients with less disease, but it wouldn't be because of the regulatory process, from my viewpoint.

DR. HARTZ: But if they could be used very easily, they would be used, if the regulatory process made it --

DR. FEARNOT: I don't think this change -- I don't think a downclassification changes it from the clinician's viewpoint unless someone has some rationale for that happening.

DR. HARTZ: Okay. One working basically under this risk section, the way to create a false aneurysm in an artery has traditionally been to blow up a Fogarty catheter in a lab animal. So the issue has been addressed, and it was casually mentioned in your protocol, increasing incidence of aneurysms.

So is it really the guide wire or is it the high inflation pressures? But that's the way we would in an experimental animal create an aneurysm. So I think I agree again with the concept, we haven't seen all the risks yet, and that's of some concern to me with these high inflation pressures, something we should be thinking about.

Then just minor housekeeping things again, like he said. Here in one point in your protocol you say angioplasty is compression of plaque. In another portion you say it's creation of an arterial injury.

So I think it depends if you are

performing a low pressure angioplasty, yes, you might compress some plaque, and that's got a high incidence of restenosis. But if you really get into what you are talking about, treating the lesion definitively, it's not that effect.

Then I have some little things on the risk section I'll add maybe this afternoon.

ACTING CHAIRPERSON TRACY: I think we are close enough to the 12:15 point that we will break for lunch and resume at 1:15.

(Whereupon, the foregoing matter went off the record at 12:14 p.m.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:22 p.m.)

ACTING CHAIRPERSON TRACY: Okay. I would like to resume the open committee discussion and turn the questioning back over to Dr. Hartz who, I believe, still had a couple of things to discuss, and the industry reps can take their seats.

All right. Then I guess it comes to me. I just had a couple of quick questions, I think.

I need some clarification maybe either from the FDA or from you regarding the issue of in-stent restenosis. I'm a little concerned that we really don't have a database that would support exactly what the risks would be associated with that.

I don't know whether a special statement should be made in the identified health risks or whether that would be some separate area in the guidance document that could be specified that we really don't know what the risks are. I was wondering if we could have some comments on how that would fit into the picture.

DR. FEARNOT: Let me just start. The area

of in-stent restenosis was not very deeply addressed in what was submitted, and I would certainly agree with that.

I think there is the possibility of looking at several of the clinical trials that have dealt with in-stent restenosis and have PTCA arms and be able to answer that question today. But I think it is going to take more review than what we have done so far to look at that issue and come to a real conclusion on whether the risks are really any different than angioplasty inside vessels without stents.

MR. DILLARD: Jim Dillard. I guess I will answer back with maybe giving you a couple of things to think about or a couple of tools, which are, I think, especially based on what the sponsor just said, that if you as a collective group do not feel that it was adequate in terms of addressing both the safety and effectiveness of data issues associated with that particular patient population, that would be something that you would want to work into your recommendation as to how strongly you think it should be either

advocated or removed from what you think would be appropriate for a recommendation of reclassification.

So I think that is one of the things you want to consider and, I think, is an option to either include it or to have it by way of recommendation as there isn't enough in the petition to support it. I think both of those options are available to you.

ACTING CHAIRPERSON TRACY: To potentially separate out in-stent restenosis, but that kind of puts industry in a bind in terms of reclassification if they are -- Currently, there are no specific guidelines in terms of the use of balloons for in-stent restenosis.

So are we creating a conundrum by not including this within the reclassification? Are we creating some kind of a problem of future products?

MR. DILLARD: I think it would -- Jim Dillard again. I think it would be creating a situation where both the agency and manufacturers as well as the clinical community would have to take a look at those products that potentially would otherwise come through that mechanism of 510(K) pre-

market notification, if these devices were reclassified.

Then they would look different in terms of the labeling from what you currently have available as those PMA approved PTCA catheter products.

ACTING CHAIRPERSON TRACY: Okay. The other -- Did you have another comment on that?

The other issue is that there are now balloons that incorporate other additional features for drug delivery and so on, and I would assume that it would be specifically recognized and should probably be specifically stated somewhere that we are not talking about reclassifying devices that are used for different types of injection pouts and so on and so forth. I'm assuming that.

DR. FEARNOT: That is right, yes. That also fits in the regulations for 510(K)s. If there is a technological difference, then that causes several more reviews to be looked at and more issues to be looked at, and I think, in terms of drug delivery balloons, etcetera, those are all still PMA and would not be included in the reclassification.

ACTING CHAIRPERSON TRACY: Okay. In your comments you often refer to the guidance document, which clearly needs some updating in terms of meeting the specific issues that were addressed. I think that that is appropriate to update it and an appropriate reference to make, but it would need to be looked at pretty carefully to make sure those are all covered in there.

The only other problem I am having is identified health risks, and a couple of other people have brought this up and mentioned air embolization, infection and removing balloon rupture and guide wire fracture.

I guess I'm not sure what the list means by identified health risks. You know, a failed procedure is a health risk or is that -- What is the intent of this list?

MR. DILLARD: Jim Dillard. I guess I will jump in on that one, since it's a procedural issue.

The statutory framework and the regulatory framework that we have to work in for reclassification designates that we identify all known risks associated

with a product and that, in order to differentiate a Class III and a Class II product, special controls would need to be developed that will mitigate the risks associated with that particular product type, and that then those special controls would adequately and appropriately ensure the safe and effective use of those products, and the regulation of those products with those controls applied.

So I know that is maybe some regulatory jargon to basically boil down and say that, in order for it to be a Class II product, we have to know the risks, and we have to specifically have a special control associated with one of those risks.

So it is part of the regulatory exercise we go through in order to say here's the known risk, and here's the special control associated with it; therefore, it can be appropriately recommended for Class II. That's part of the procedure we actually have to go through.

ACTING CHAIRPERSON TRACY: I think I would favor keeping that list a little bit broad, since it is very difficult to distinguish between a product

risk and a procedural risk. Certainly, the balloon is not causing a coagulopathy, but the coagulopathy is associated with the procedure in which the balloon is used.

So I would sort of favor keeping things a little bit broad from that perspective. That was all I had. Dr. Crittenden?

DR. CRITTENDEN: I wanted to ask -- I'm sorry, I'm going to be informal -- Cases, what percent of the time in your practice do you perform just angioplasty alone without deploying a stent?

DR. PINKERTON: I think that I would say probably about 30 percent.

DR. CRITTENDEN: Thirty percent of just pure, kind of primary PTCA?

DR. PINKERTON: I think we are tending to go recently to just primary angioplasty for small vessels, and the data has been kind of iffy on using stents where the vessels are small, 2.5 or less millimeters in size.

DR. CRITTENDEN: Is there a difference in the balloon characteristics if you use the angioplasty

catheter to deploy a stent?

DR. PINKERTON: Really, no, as a rule.

DR. CRITTENDEN: So they are essentially the same catheter. When you go to pick a catheter, when the nurse goes to get it, whether you are doing primary angioplasty or deploying a stent, it's the same catheter. There is absolutely no design, engineering --

DR. PINKERTON: No, there is not, really. No, no.

DR. CRITTENDEN: -- change whether you use a semi -- what was your word?

DR. PINKERTON: Semi-compliant.

DR. CRITTENDEN: -- semi-compliant. It doesn't make a difference?

DR. PINKERTON: No.

DR. CRITTENDEN: Then any of the studies that Dr. Fearnot talked about in his presentation, they include patients who received stents as well. There was one that your Powerpoint slides talked about, all the different, I guess, long term --

DR. FEARNOT: Most of those studies did

not include stent, and I picked earlier studies to try to separate out studies done for PTCA directly. Obviously, they are a little bit dated, because today's --

DR. CRITTENDEN: Right. Well, I guess those are the ones you really have long term data for.

DR. FEARNOT: Right. I think today's -- many of today's or the recent past's stent studies have had a control arm of PTCA patients from which we also obtained data, but those old studies were chosen because they didn't -- they were mostly comparing just PTCA with surgery or PTCA alone in a series.

DR. CRITTENDEN: Well, I bring it up because I had some concern over the statement you made, and it may be paraphrasing it incorrectly. But I just kind of wonder if we have enough data to support the claim that dilating in-stent restenosis and untreated coronary stenosis or a maldeployed stent are really the same thing. Is that what I understood you to say?

DR. FEARNOT: You did understand that, but I don't believe the data that I showed you in the

slide supports that. It doesn't provide adequate -- I'm not saying it speaks against it either, but I think, based on this discussion, we should provide the agency with the recent trials on in-stent restenosis, and I think that those data would stand.

DR. CRITTENDEN: Dr. Pinkerton, do you think those are the same things, those three phenomena?

DR. PINKERTON: As far as --

DR. CRITTENDEN: I'm sorry. Do we have enough data to support the claim that dilating in-stent restenosis, untreated coronary stenosis or a maldeployed stent, that those are all similar types of things in terms of the mechanics of what is being --

DR. PINKERTON: Yes. I think, you know, from the other trials that have been done where the balloon has been the control arm for in-stent restenosis, there really has been no significant difference between the new technologies, either in complications or in the success rate.

DR. CRITTENDEN: And then, Dr. Fearnot, do you think there will be a change in the innovation

with this if we go -- If we reclassify it, will there be less or more innovation in terms of technology, either making it better for the patient, less errors, less problems, or easier for the clinician to use?

DR. FEARNOT: I would suggest that it will have very little impact whatsoever on the clinical practice of medicine, on the number of angioplasties performed, or on the outcome of those angioplasties. I really believe --

DR. CRITTENDEN: I'm sorry. I meant to talk about balloon technology. Will more companies enter? Is this because it's easier, there's less of a hurdle, or there will be more people coming up with new techniques, new balloon designs, etcetera, to make the process better or are we going to make it worse by letting anybody come in and do it?

DR. FEARNOT: I don't believe there will be any detrimental effects. I do think and hope that what it does is frees up FDA staff to focus on newer issues. Now they won't be newer balloons but, for instance, coated stents and brachytherapy and the other new interventions that are coming forth really

do deserve a significant amount of attention from the agency as well as the medical community and the industry to make sure that those new techniques are available as rapidly as possible and as safe as possible.

So I think that's the benefit out of this. I really think it will have very little impact, if any at all, on balloon manufacturers or the development of new balloons.

DR. CRITTENDEN: Finally, the MDR and MAUDE reports -- do those just talk about primary angioplasty or do they talk about primary angioplasty, in-stents, those adverse events that are just for pure angioplasty?

DR. FEARNOT: They include both.

DR. CRITTENDEN: They include both?

DR. FEARNOT: Yes.

DR. CRITTENDEN: That's all I have.

MR. DILLARD: Jim Dillard. Just one point, I think, for Dr. Crittenden's sake, of clarification and that being that the stents that are currently approved for coronary applications are all

pre-mounted stents.

So from the standpoint of initial stent deployment, what we don't have is we don't have bare fiber balloons being used for stand-alone stents, crimping it on and then being approved for coronary applications. That's not the current state of technology nor how we regulate the products, not that that is impossible to envision, but isn't currently the way the technology is.

DR. CRITTENDEN; So when we reclassify this, then we are not addressing those pre-mounted catheters?

MR. DILLARD: Correct. They are their own product type.

ACTING CHAIRPERSON TRACY: Before we move on, let me just go back to Dr. Hartz.

DR. HARTZ: Hartz, Tulane, again. Under potential risks, I would say under arrhythmia "life threatening arrhythmia." Under embolism, I would say "to the heart or to any artery in the body, specifically aneurism formation in the coronary, the artery being treated.

Under vascular access, site complications and guide wire complications, I would say "may require surgery" -- "perhaps requiring surgery." That's the first thing.

The only other thing is from then on there are numerous references under your complication list to causes and prevention and treatment, and allusion is repeatedly to, quote, "practice of medicine." I don't see that as a control.

DR. FEARNOT: I would agree.

DR. HARTZ: I see it as an anti-control. So I don't know. Jim, from your point of view, is that an approved FDA way of --

MR. DILLARD: Well, I'm not sure what an anti-control is.

DR. FEARNOT: I was trying to allude to the fact that there is the practice of medicine which, really, the regulatory process has little effect on in general and that there are some practice of medicine issues. Then there are regulatory issues. In order to make a sensible approach to reclassification, to some degree you have to look at the regulatory issues

related, obviously, in the context of medicine. But really the regulatory process itself cannot and should not address many of those practice of medicine issues.

DR. HARTZ: That is specifically why I think it shouldn't be in there.

DR. FEARNOT: Oh, okay.

ACTING CHAIRPERSON TRACY: Dr. Aziz?

DR. AZIZ: Like my other colleagues, I, too, enjoyed the presentation. I think it was quite informative, and I think a lot of the good questions have been asked, but I might just focus on one or two things.

If I understand correctly, because most of the procedures nowadays involve angioplasty plus a stent placement, so by reclassifying the procedure it will only impact a very small percentage of patients. I mean, you mentioned that in your group 30 percent. So it really probably won't have a major impact unless, obviously, the whole angioplasty scene takes off even more.

A couple of questions from the surgical perspective. Most of these angioplasty catheters

obviously are used for dilating the native coronary artery or saphenous vein grafts and, I guess, a smaller number for an IMA or maybe the arterial conduits that may have a problem.

Do you have any information on that?

DR. PINKERTON: With this, I am just going to have to talk about some isolated studies. But usually, when the arterial conduit is involved, it is usually involved with the distal mass stenosis. Now I mean the shaft of the arterial conduit very rarely, the IMA or whatever very rarely is treated unless, you know, by some fluke.

There have not been any studies that I know of with stenting that area, but historically speaking, distal mass stenotic lesions really do better with TVR than native vessels, as a rule.

DR. AZIZ: So in case that we have a string sign, it may be because of competitive flow in the native IMA --

DR. PINKERTON: Right.

DR. AZIZ: -- where you may have to dilate the whole length of the IMA. Have you done that?

DR. PINKERTON: I do not believe that that really is being done in any significant amount, because usually we approach the native vessel in that situation.

DR. AZIZ: Obviously, the nature of the vessel is much softer, and so the propensity for injury, particularly rupture, and it would be quite significant, I think particularly when you are focusing on just dilating rather than putting stents along the whole length.

DR. PINKERTON: Well, usually in that kind of a situation when you have an atretic intramammary, the native vessel is open, and usually from an interventionist point of view, the native vessel is addressed.

I don't know -- I can't say whether long term that is better. Maybe we ought to close the native vessel and let the mammary reopen, but those are issues that I really -- there is no data on that I can answer.

DR. AZIZ: Did you have any -- Obviously, a much smaller number of patients get allograft

conduits, you know, if the saphenous vein is allopreserved or something. Do you have any information on how angioplasty affects those veins versus just the regular saphenous veins?

DR. PINKERTON: Well, of interest in my -- I have only had two cases in my career, but I haven't seen many things published on it. But the cases that I have done, I have done, I think, a total of five Dacron grafts, and they are usually very hard to dilate, and they aren't really -- As far as I know, there aren't many people that have those that are -- you know, it's not a routine surgical procedure. But the balloon angioplasty catheter works the same.

DR. AZIZ: One last question. Obviously, I think the vast majority of these cases are adult cases.

DR. PINKERTON: Yes.

DR. AZIZ: There have been scattered reports where young kids with Kawasaki's disease --

DR. PINKERTON: Yes.

DR. AZIZ: -- have had angioplasties done where the catheter is obviously much smaller, and the

long term outcome -- I mean, the idea being to allow the heart to grow so you can do something. Could you shed some light on your experience?

DR. PINKERTON: Yes. It's very interesting. We just did a five-year-old boy six weeks ago with an allied lesion, and we actually used a Rotoblader because the vessel was very calcified. Then we followed it with low pressure balloon angioplasty and didn't put in a stent, and he is due for a restudy in about, you know, six weeks.

We had to design a special guiding catheter and so forth to get the case done, but the procedure really went just about like an adult.

DR. AZIZ: Maybe one last question. Another entity which is somewhat unusual where the intimal hyperplasia may be of a different characteristic but still, I think, is probably response to injury, transplant atherosclerosis where you really have concentric lesions all the way down, different from, you know, the regular atherosclerosis we have with a focal lesion.

DR. PINKERTON: Right.

DR. AZIZ: What is your experience? Do you think angioplasty catheters may have -- Better angioplasty catheters may have better outcomes?

DR. PINKERTON: I really don't think so, because I think it's based on the pathology. I think, you know, the longer, the more distance that you dilate, the higher the chance for recurrence.

I know, as far as restenosis, we did a trial with pathologic specimens that we published, I don't know, about seven years ago, and we retrieved intimal proliferation from all types of interventions, including stents, rotational atherectomy, directional atherectomy, and balloon angioplasty.

Microscopically, the material was the same.

DR. AZIZ: In all those?

DR. PINKERTON: Yes, in all those. Yes.

DR. AZIZ: Interesting. Thank you.

DR. SIMMONS: I really don't have any really hard questions. I thought the packet was pretty straightforward, very nicely put together. The presentations were all very informative.

I just didn't think it was much of an issue, and I also was getting gestalt from the FDA, hearing their presentation, that they didn't have much of an issue with it either, and not being a plumber, I don't have a lot of real insight into catheters and balloons and stuff.

I guess I had one informative thing that maybe you could help teach me. I know the FDA with their treatment of generic drugs, as a cardiovascular arrhythmia person, less than spectacular history with, you know, 20 percent less or 30 percent more, that's good enough, and that -- I mean, certainly, with arrhythmia drugs and anti-coagulants that is really not good enough.

I have had sort of backtracked on the whole idea of using generic drugs a lot. Are we approving a generic catheter here that is now going to have less controls, less rigid specifications in the long run?

MR. DILLARD: Good question. Jim Dillard. I don't see Dr. Fearnot jumping right in for this. So I guess that is to me.

I don't know that I would look at it that way. I think that -- and my background certainly is not Center for Drugs. So I am not going to comment on what their differences perhaps are between their generics and their original drugs.

This is not uncommon for us in the world of substantial equivalence. Let me give you sort of my vision about how we approach products in 510(K), which if we have an established set of criteria that seem to define a device type and that criteria could include both bench types of information, animal information, as well as clinical information, that help us understand sort of, quote/unquote, "a generic" category of products -- and I use that terminology loosely -- that when we start having an understanding of those product types, that's what defines an area of a Class II product.

So if a product falls within the general understanding about preclinical performance, bench performance, animal performance, the next step at least in terms of device logic is to say that the safety and effectiveness can be subsumed or can be at

least understood based on comparison of other information that isn't necessarily clinical information.

So we do in a product area that is defined by these characteristics get a feel of how the product is going to perform, and that is generally what we would consider, I guess, as maybe our corollary to a generic drug. It is really the class of devices becomes something that is definable by certain preclinical and clinical kinds of information.

So it isn't so much a generic. We don't prove within a bioequivalence range, for example, that a drug product is 10 or 15 or 20 percent away from what the original product is. It's more of an overall class or category view of the product type.

That is probably as close as I can draw by way of comparison of how we look at the category. Just because it becomes Class II doesn't mean it becomes, quote/unquote, "generic." It more defines a category of class that then is regulated differently, and then doesn't have to be proven a priori with its own safety and effectiveness information that it has

reasonable assurance of that safety and effectiveness.

Some of it is built on additional other information. It isn't only clinical study data. So I don't know if that helps or not, but that's how we kind of view the 510(K) process.

DR. FEARNOT: Well, let me just make a couple of comments, as one who has written over 100 510(K)s personally.

I can tell you that FDA asks for clinical trials for even a 510(K) process application about ten percent of the time. I believe that is still current, roughly. So there is a clinical trial involved about ten percent of the time.

There are animal studies generally required in approximately that and maybe a little bit more than that percentage of time. So I think that in no way do I see this as making it sort of a generic category, but it is a product area that you can describe the risks for, and then put in place a guidance.

So I am really asking myself two questions. One, do we understand the risks well

enough to describe them and to look responsibly at gathering the data to minimize those risks, providing the data to minimize those risks, providing techniques to minimize those risks?

Secondly, today if you have a catheter that has the general characteristics of the balloon catheters -- for instance, at eight atmospheres it inflates to a diameter of three millimeters -- will that catheter at three millimeters and eight atmospheres do the same thing another catheter would do at eight atmospheres at three millimeters? And I believe we are at that point where we understand that.

Now there are finer details, as Dr. Krucoff mentioned, regarding the tip and some shaft issues, and the manufacturers deal with those constantly and work on those. So there is testing to cover those and make sure that those finer details also are -- but I think in terms of the reclassification, I don't see it as a generic versus nongeneric drug issue, but rather a matter of saying we understand the risks, we can put certain controls in place to notify of those risks, provide data to

minimize those risks, and then rely more heavily on the fact that, if the characteristics are the same, then the risks should be the same. So that's where we sit today.

DR. SIMMONS: Things like you were describing, like the three atmospheres and it dilates to a certain diameter and it has a certain compliance curve and it has certain stiffness of the shaft, who does that testing and provides that information?

DR. FEARNOT: The manufacturer does the testing and provides it to FDA before they will review the application.

DR. SIMMONS: Does the FDA review the testing procedures?

MR. DILLARD: Jim Dillard. Yes and no. Yes, if the manufacturer comes to us early enough to ask for comment on those particular procedures or protocols. Then yes, we will comment.

Quite frequently, however, if it is a well understood area of bench testing, for example, a lot of that information can be gotten from other sources other than the FDA, and so once a technology becomes

established, I think we are involved less and less with designing protocols as they become more and more standardized, more and more well published, that sort of thing.

So yes, only if the manufacturer comes to ask us for input into the protocol.

DR. FEARNOT: Let me clarify one thing. The FDA sees the methods. What Jim commented on was whether or not they were involved in writing the protocols. Many of these protocols, biocompatibility protocols and several of the testing protocols are pretty well understood and well developed, and honestly have been used for some years.

So there is very little input either from industry or the FDA to change those testing protocols. So that when those data arrive at the agency, it says we use this method, we arrived at these data, and they understand what the data are and the method used to obtain those data. They are reasonably self-explanatory for a well developed method.

DR. SIMMONS: Okay. I guess what I was sort of wondering is like a start-up company and a new

company. You are trusting them to build the catheter, but you are also trusting them to design and do the testing that provides the data to the FDA that the catheter is really okay.

So is that like the chicken house being guarded by the wrong person?

DR. FEARNOT: I don't believe so. As someone who has received lots of deficiency letters, some of them have had 40 and 50 questions on testing methods. I think the reviewers are pretty responsible in terms of asking questions. Some days I would like them to ask fewer questions, but I tell you, they ask quite a few.

ACTING CHAIRPERSON TRACY: Dr. Li?

DR. LI: Yes. Steve Li, Special Surgery in New York. Thank you for your presentations. Both were very interesting.

So my focus and role in these things is the materials and design person. So I mean, I kind of step out of the clinical sense for a second and ask some questions, I think, that I am curious about.

One in definition: I'm curious of why you

described the balloon as being constructed from a high density polymer. Of all the polymer properties that one could have characterized your material, why do you pick high density, and what is high density?

DR. FEARNOT: Well, perhaps that suffers from being a little bit in terms of jargon. But there are balloon catheters such as Fogarty-type catheters, urinary catheters, you know, that have latex balloon material. So there are other classes of catheters.

I had a slide that I didn't present, the other classes of balloon catheters that wouldn't fit the PTCA description or definition. So what we were trying with the high density polymer wording was to avoid that class of devices, the ones with latex or silicon rubber or those other balloons.

DR. LI: So what do you think high is then?

DR. FEARNOT: One that basically is pressure driven. It's a material that can withstand pressures in the ranges we are talking about without major expansion. For the basic control mechanism of latex balloons and silicon balloons, it's more or less

a volume control, if you will, because the volume injected controls the size of the balloon, and really it doesn't generate a significant amount of pressure.

So perhaps, you know, we can use other wording that would better describe it, but the goal was to get to those materials -- limit it to those materials that are more pressure driven where the volume is fixed and the pressure rises rather than the volume increasing and the pressure staying relatively the same.

DR. LI: I understand your intention, but as a materials person, this is particularly nondescriptive. In fact, one could take the latex type material, which by itself is rather soft and, I guess, in your jargon would be low density. There are constructs you can make of that that are actually rigid.

So it's a combination of the design and the material, and certainly density is a particularly poor characteristic to use as the delineator. So I understand your intent, and your intent is fine.

DR. FEARNOT: You'll need to recommend a

better wording.

DR. LI: Yes, if I can do it in something as short as high density, I could. I'll work on that. But I think it's particularly misleading, especially if you are going to use it in an exclusionary fashion or an inclusionary fashion as the primary definition of the device.

As far as the compliance goes, there was a chart, I guess, in the presentation. I guess this is kind of back to, I think -- I'm not sure who raised the issue about the definition of minimally compliant.

I am troubled by kind of, again, the kind of soft usage of the word. For instance, in the presentation you had one chart that showed the difference between a more compliant and a less compliant balloon, but if I actually put those lines on the chart below it, they are actually off the chart below those lines that you say represent the compliance of typical various PTCA catheters.

So there is a huge variation in compliance, and I am not quite sure what minimally compliant -- or why any reflection to the word

compliant means, unless you are going to be a little more specific, again unless you meant to exclude or include something there.

If you had meant to exclude things like urinary catheters, I would propose you do it with an actual engineering specification, which are probably at your beck and call, rather than use words like minimally through that.

DR. FEARNOT: I would say that there is a range of compliance that is typical of balloon catheters. I think Dr. Pinkerton made two points. One is some of these materials in the way they are constructed provide a lower range of pressures, and other constructs provide a higher range of pressures.

Secondly, almost independent of the burst pressure or the maximum pressure, there are noncompliant, and that's the jargon term in the field, or semi-compliant balloons. None of them are highly compliant.

So there is some attempt to use compliance, which is a measurable property, to categorize this class.

DR. LI: Just as a materials and engineering standpoint, I think I would prefer to see actual specifications and numbers. So you take it out of the interpretation arena.

I have a couple of questions related to the MAUDE/MDR numbers that you supplied. Most of my experience has been in the orthopedics in the last ten years, but I can tell you from the orthopedic standpoint, the MDR and MAUDE, although they are indicators like Jim Dillard said of problems out there, in some cases it is estimated that the number of device failures that get reported is somewhere on the order of one or two percent of the actual number of failures.

So there are institutions that do thousands of total joints for decades that have never made an MDR report through this, because when the manufacturer gets it, they are required to make the report, but the hospitals actually aren't mandated to turn everything over to the manufacturer, and therein is the disconnect.

So with that preamble, do you have any

concept of what the number actually is of devices that fail versus what get reported?

DR. FEARNOT: I don't. I don't have data on that. I don't think the data is really obtainable.

DR. LI: Because I was looking through your references also, and just reading through the titles of your pages of references, I actually didn't even see a paper that alluded to addressing that issue. So the concept here is we actually don't have any idea what the actual number of failures -- device failures there are.

DR. FEARNOT: I think that is true. I think that would be -- that is misusing that database, in a sense, to try to get that out of there. Part of the problem is the denominator problem. As you know, statistically it's almost more difficult to get the denominator than it is to figure out what percentage of the cases are actually reported.

DR. LI: I raised the issue -- Oh, I'm sorry.

DR. FEARNOT: What the data does provide, though, is a listing of sort of surveillance data, if

you will. in other words, if you look at those data, you can look through and determine whether or not there are any new adverse events.

You may not get the incidence of the events correct, but you do typically identify some of the more bizarre events related to medical devices, and in that you can go back and check and see if the list of potential adverse effects is adequate or not or whether there are new -- As Jim said, there's also all of a sudden a burst of a certain type of a problem, and those databases are used for that and are appropriate.

DR. LI: Well, understood. But the section where you allude to perhaps the devices are getting better because the number of reports is dropping, really, that's kind of a stretch -- right? -- given the fact we have no idea how many are actually getting reported or the reasons they are getting reported?

DR. FEARNOT: Yes. I think that the data in the MAUDE database is the wrong data to support that statement. I think there are other studies,

though, that do support that statement.

DR. LI: Were those included in your filing?

DR. FEARNOT: I would have to look particularly at the studies.

DR. LI: Okay. A question, I guess, on the use of the guidance documents or to look at the mechanical test that the guidance document suggests that you do, which is relatively inclusive.

I'm a little taken back of how nonspecific each of those tests are. Typically, with other medical devices, if there is a test, there is actually a kind of a, in some cases, overly specific description of the test, number of samples, the loading conditions, you know, right down to a sketch of the actual test.

It didn't seem to exist for actually any of these tests. There are no ASTM references. There are no ISO standard references to this. Then I couple that with, I guess, one of the tables that Dr. Pinkerton provided that showed that the maximum recommended pressure for use is something on the order

of 40 percent less than the minimum burst pressure that the balloon is rated for. Yet we still get balloons that burst.

So if this was an accurate representation of the clinical situation, really, the number of balloon bursts that you get should be near zero, but in fact it is somewhere above zero. We don't know how big that number is.

So although the list of tests is lengthy, can you comment on the link between those tests and a clinical performance? I'm going to complicate that question a little bit more, because one of the things I'm worried about is the future.

In other words, there is a set of products with the design and materials you are using now, but I don't think you should underestimate the creativity of the materials and engineers people will continue to get new versions of things that we don't currently anticipate.

So how can you comment on the appropriateness of using these unspecified, kind of always evolving kind of mechanical tests in relation

to a clinical performance?

DR. FEARNOT: Let me show you first that every one of those tests has a very detailed protocol. As you know, from an engineering standpoint you can't run the test unless there is a protocol. So I didn't feel like I had the time to go through all the engineering process. I really didn't think it would be of much interest to most of the panel either.

DR. LI: I am probably the only one that cares, in fact.

DR. FEARNOT: Well, I would love to talk to you quite a while about it, but I didn't want -- I wanted to respect the time that is available today.

There is a test protocol or method for each one of those tests, and so the data only meaning as much as the test protocol is specified, as you know. So I didn't mean to connote that there was not a test protocol for each one of those tests.

DR. LI: Maybe just a short question to the FDA. If someone comes in, anybody comes in, with one of these balloons that we are considering reclassifying, is there, for instance, a standard

burst test that you ask everybody to do or do you kind of tweak the test a little bit, depending on the device?

MR. DILLARD; Jim Dillard. There is not a truly standard test for any one of these that we could point to to say either we have written a performance standard which includes real performance specifications or is there an industry based standard that we could point to.

I think, over time, however, what we have tried to do is utilize our knowledge each time and feed that to the company when they are designing their tests, so that what we can come out with is many bench tests that look similar, although not identical necessarily.

I think part of that speaks to in this particular area where we have what we are calling, quote/unquote, "a standard" balloon, but as you probably well understand from the guidance document, it is written more broadly than just to encompass this particular type of balloon.

So the broader we get in a guidance

document, the less specific we can get on the tests. I think that is really just a factor of this particular guidance document. Not that some of those couldn't be written, but I think the way we have them, we just haven't written them that way.

DR. FEARNOT: I think the agency has put out some guidance and gives guidance, and so that there is a reasonable consistency. For instance, minimum burst pressure, there are calculations in guidance saying this is the equation to use, this is the way to calculate it.

Obviously, you have to do a statistical sampling method, some method that has enough samples in it so that the data are meaningful. So in submitting the data, not only are there the actual data but there are methods and the statistical rationale for the number of samples being treated. That does vary to some degree based on, you know, statistical parameters estimates of the air and that sort of thing.

Let me address the balloon issue with regard to rupture a bit, because to some degree, no

matter how good the materials are, we will never arrive at 100 percent. That number of 100 percent of the devices will never fail is just one that I am comfortable with.

The balloons, though they are rated such that 99.9 percent of the balloons will not rupture with a 95 percent probability, nonetheless, that is in a rupture due to pressure without consideration of the sharpness of the spicules of calcium in the vessel.

It would be virtually impossible to look at the spicules of calcium and make a plastic balloon that under no circumstances would rupture, given how sharp those are sometimes. However, today the number of ruptured balloons really is not all that high.

What we've seen is that there isn't a direct relationship between a balloon rupture and vessel rupture or dissection, although there is obviously some connection.

So I think, while we can make sure -- and it is reasonable to make sure -- that only one in 1,000 balloons with a 95 percent probability would rupture at their rated pressures, I'm not sure that we

will get much closer to testing against spicules of calcium, that sort of thing.

DR. LI: I wasn't so much speaking behind that. I don't want to beat a dead horse here, but I guess one of the things that seems -- Again as a materials person looking at device testing, what I don't see is what I will call, for instance, combination testing.

So it could be that, if you just take a brand new balloon out of the box and do your burst test on it, it is in fact quite well within the limits. However, I'm not sure what the -- I'll just make up a scenario.

Perhaps, though, if you inflated or deflate it a number of times, that number changes. So references to the rate of inflation affecting the burst. So maybe if you do a slow one, then a fast one or -- I mean, in other words, I don't see any combination testing in there, and perhaps it is that combination of treatments to the device that leads you to a higher burst rate than one would normally expect, just based simply on rupture pressures.

I don't see any kind of allusion to that particular type of testing in here. Again, this is more -- not so much aimed at the current product, which I'm not quite sure what the burst rate is, but I will just assume for the benefit of the doubt that it is relatively low. But I'm more concerned with what folks like myself could dream up a we come down the pike here where we don't exactly know -- I guess this was one of the earlier comments, that it's an ever evolving technology, and we are not quite sure essentially what the cross-factors are.

So it could be, if you make it thin, you deflate it, put it against a stent, you get a higher breakage rate. I mean, I don't know. But there are combinations of factors that are stacking up rapidly in here that none of the testing is actually aimed at finding out.

Again, you know, maybe it's safe; maybe it isn't. I'm just pointing out what I think to be kind of an obvious hole or at least a deficient area.

DR. FEARNOT: We do combinational testing. There are repeat inflation tests, etcetera.

DR. LI: But then do you do a burst test after?

DR. FEARNOT: Yes. We do a burst test after.

DR. LI: I guess maybe this is back to my part into the guidance document on the mechanical side just seemed a little --

DR. FEARNOT: It's a little weak.

DR LI: It's a little loosey goosey, right, as far as I'm concerned. If this were to go forward, I think I would like to see details of testing, really no more than other devices have in their terms of specificity and range of testing.

Then just as a last item here. The thing that isn't mentioned are sterilization and shelf age effects. For instance, any of these products that are gamma sterilized have a shelf age issue on them, but I don't see any allusion to aging and performance of these devices after whatever shelf age they may see, just as examples of things that appear to be missing out of the guidance document.

Let me just reiterate this last thing. I

just don't think anybody can underestimate the creativity of those people that will try to improve this device. It just happens, it's our history of medical devices.

You find what you think is a deficiency in a device. You aim for improvement of that one specific factor, and because we don't know all the other co-factors that are tied with it, we kind of slip off somewhere else.

Again, this is more related to a future problem, but that kind of relays into this issue of reclassification, not so much that it is inadequate for the current product, but if we downclassify, how to ensure these kind of things don't happen in the future. Thanks.

ACTING CHAIRPERSON TRACY: Do either Mr. Dacey or Jarvis have any comments they would like to make at this time?

MR. DACEY: Just briefly, of course, it is always hard. You know, what does a consumer say about all this?

Well, first of all, when I get my

homework, I do pour over all the information. Part of this is my own training, but it's always gratifying to hear questions asked that I had marked to ask. So I guess I'm doing the right thing.

In my work in patient education over the years, as a patient myself, you know, it's sometimes hard for consumers who get their information from "ER" and CNN and news bites to understand what I come away from every one of these meetings, and I wish I could capture it for the consumer, because I hear over and over again the issue of not harming the patient.

I don't think the consuming public really has a good understanding of that at this level. So when I go back, I see a lot of stent patients. People put a great deal of faith in the work you are doing, the work of the panel. They make a real lap of faith.

It's for the most part justified. So when I do go back and I deal with patients, one of the things I try to impress upon them is the fact that, by my own experience working with you folks, I'm seeing the fact that it's their best interests that are at the center of all the effort.

On the future, referring to the future -- I was reading on the plane coming in about the digital technology and GPS. Is anybody working on stents that can be monitored by GPS so the patency can be reported back to a central control, because from what I read, that's not too far away.

That's all I had.

MR. JARVIS: I have nothing right now.

ACTING CHAIRPERSON TRACY: Any other questions from the panel?

DR. KRUCOFF: Mitch Krucoff. I just wanted to follow up real briefly on that clarification from Jim to Dr. Crittenden that a stent delivery system is pre-mounted, but the balloons we are talking about -- that stent is then likely to be post-dilated.

So I think there is room -- and that would be done with an off-the-shelf balloon that would fit into these. So I just wanted to be clear to everybody that we do have a lot of device interaction potential with balloons that come through this path.

DR. LASKEY: Warren Laskey again. And to follow up on something that Dr. Li made me think

about, it is a given in this business that there is a gap between the in vitro performance and the in vivo performance, what you measure in the bench and your mechanical characteristics and your compliance. They are vastly different in the body. That, at least, is my understanding.

So given this gap -- and we don't really have a handle in terms of standards for the in vitro characterization of the behavior of these instruments. Given the gap between the in vitro of the bench and the in vivo performance, can you at least speculate about the likelihood that this gap will widen with a new classification schema?

DR. FEARNOT: I don't think the gap will change. I think the in vitro testing is specific to what the device will do under its various conditions mechanically. I think, as it is used in vivo, if you were to inflate it at that pressure, it would still meet those same criteria.

I think the gap you are talking about is that those mechanical performance characteristics of balloons don't translate into -- directly into any

particular medical outcome that is directly related to the balloon characteristics.

You know, a three millimeter balloon in one vessel may have a perfect vessel. In another vessel, even though the balloon performs identically, it may have a different result. That's a gap that I don't think can be addressed with in vitro testing.

I think there have been clinical results to describe what the outcomes will be in general, and I don't see, if we do a decent job on the guidance -- I don't see that gap widening, because I believe the tests that we use today have been used for several years, and have characterized it.

I think the clinicians look for compliance curves. They look for burst pressures and, given those pieces of data, they are able to perform the practice of medicine.

So I don't see that testing of any kind on a balloon catheter will address some of those outcome issues, but I don't think there is anything in a reclassification process particularly that will widen that gap.

DR. LASKEY: Well, let me get a little bit more specific. If you will, the poor man's compliance definition, the pressure/diameter relationship in the bench on a balloon is not what it is in the body, at least in the studies that I have seen where people have done P-D relationships.

That's what concerns me, that because there is this relative lack of consistency, if you will, between out-of-the-body and in-the-body performance and, similarly, with the rate of burst pressure issue, but more to the compliance issue which is a strict mechanical definition. It's the slope of the pressure/diameter relationship.

That's different in the body than it is in the bench.

DR. FEARNOT: Yes. I think for years clinicians have translated from the printed data in terms of the compliance chart and what they can expect in various types of lesions. At the higher pressures, obviously, the balloon pressure is dominating most of the relationship.

So as the pressures increase, I think you

will see the pressure/diameter curve matching very closely to the compliance curves shown in a chart, but for low pressures, obviously, the lesion is dominating a large bit of that. But I think over the years you will see that, form a protective standpoint, with those compliance charts I don't think we see -- we don't see diameters larger than those specified in the chart at a given pressure in vivo.

So I think from a protective standpoint the difference is a matter of a lesion putting pressure on the balloon material itself, and perhaps resulting in a smaller diameter. I think from a protective standpoint, we are okay.

DR. HARTZ: Hartz again. Just a quick question. Do you know or does anybody here know what the mean or the median number of balloons per target lesion used is in any study? I bet it's not one.

DR. PINKERTON: No. I think the last thing I saw was 1.3.

DR. HARTZ: So there are a lot of patients with more than one balloon. What I'm saying is it gets at some of the questions you asked about. It's

not a perfect system, by any means.

You didn't address an A-V or C lesion, and these compliance characteristics must change tremendously with a concentric versus an eccentric lesion. So you're going to use more than one balloon if it's a complicated lesion, I think.

DR. PINKERTON: Well, I mean, this has changed a great deal since the development of stents and, you know, the secondary generation of stents especially. I think that the number of balloons being used per lesion has probably decreased.

For example, I mean, we did the study back in 1988 where we used like 2.3 balloons per vessel, and I think that our knowledge of mechanical recoil that we have developed and so forth has changed the approach to those types of issues.

DR. FEARNOT: I think also you find lesions that are tapered significantly that require different diameter balloons to treat. For instance, distally you might treat it at 2.5, more proximally 3, more proximally than that, 3.5.

So some of those numbers in terms of

multiple balloons is not a failure of the device but an actual choice on the part of the physician to treat the various segments of a tapered vessel.

DR. LI: Dr. Li again. Do you have a sense for -- Dr. Pinkerton, you said you -- You were introduced as having done over 20,000 of these procedures. There are probably --

DR. PINKERTON: I've been involved in 20,000. I've done about 10,000. That's enough.

DR. LI: Oh, okay. But still, there is some cities that haven't done 10,000. Do you have a sense for, you know, the hundreds of thousands of procedures that are done what percentage are done that say they do less than 20 or 30 a year? Is that the majority of them or is that the minority of them?

DR. PINKERTON: To be honest, I mean, there has been projections that the average number of procedures done in the United States is between 50 and 70 a year. Now I think Warren and Mitch would agree with me there.

Again, it is very difficult to separate the regulatory issues from the clinical issues, you

know. It's hard -- It's very difficult for me, because what I am trying to do and have always done is to try to design equipment that is going to be safe for someone that's less skilled than I am or less experienced than I am, because I think that's safer for the patient.

DR. LI: Where I was headed for is a question for this group, because 50 to 75 -- are there any studies that show that there are higher rates of balloon rupture or device failure in their hands than, say, perhaps your hands?

DR. PINKERTON: There is a higher complication rate, but not necessarily that.

DR. LI: Is it not studies or just --

DR. PINKERTON: No, not that I know of.

DR. DOMANSKI: Cindy, you know, actually, I think some of those questions probably -- You know, I have a problem with the raising the issue of competence of the physician. Well, let me just say, in this setting; because you know, it's like doing a clinical trial.

It's very had and probably inappropriate

to crank in -- trying to crank in something that determines what happens in incompetent hands. I mean, it's the same way with our clinical trials, particularly where they involve something other than just giving somebody a pill.

Clearly, what you say is in the hands of competent people these are the results one would expect to get. I think to try to ask these guys to somehow test for incompetence is not relevant.

DR. LI: Well, first you misunderstand the question. The question is asked in the spirit of trying to figure out what the actual rate of balloon rupture is. So again, I'm drawing on my experience in other devices where they actually have done studies, for instance, on total hips and knees, of surgeons that do less than 25 a year versus those that do over, you know, 25 a month.

Then there are device failure related criteria. It wasn't meant to be a comment on competency, but it was more a question on essentially the robustness of the device.

DR. DOMANSKI: Well, I don't -- But I

think what I would object to is putting into the equation for robustness of the device the relative incompetence of an operator, unless there were only a few people in the world sufficiently skilled to use it, and that is by no means the case with these devices.

ACTING CHAIRPERSON TRACY: Mitch.

DR. KRUCOFF: Yes. Krucoff. I really think, though, that it is key to recognize that, particularly in considering human subjects who undergo this procedure, that teasing apart what are the device related elements and what the operator related elements, is complicated.

I think we have to be sensitive to that. As Mr. Dacey was saying, consumers don't appreciate this. A lot of angioplastiers do not appreciate just how much some of the things that we are discussing here today matter, and the resilience or robustness of a device and what the regulatory path allows to come forward as a device into the market is not independent of the operators who use it, even though they qualifications of the operators using these devices

are not part of the obligation of the regulatory process.

So to me, this is a real dilemma, and I don't think we can afford to ignore it. I agree with Mike. I don't think we can allow simply the operator issues to dominate, but I agree with Dr. Li. I think there are some real issues here about what subtleties come forward in a gadget that may produce different helpful or harmful effects, depending on who happens to be using it and whether or not the change in this from a Class III to a Class II device will impact on that, because at the end of the day we are talking about people who get hurt.

ACTING CHAIRPERSON TRACY: Just a comment on that. I think there is a fair amount of data available collected from a number of users, some of whom are very expert and some of whom are much more inexperienced.

So what we have is compilation of data from a variety of different places, different sources, levels of expertise. I think, again, we are not really -- We are not regulating the practice of

medicine, and we, I would think, should make the assumption that we are talking about the standard or the median operator here as we are thinking about that.

I don't think we need to delve into it in much more detail. Are there some other comments on that, Mr. Dillard?

MR. DILLARD: Jim Dillard. Yes. I mean, I think that all the comments were sensitive to those, and I think they were all very good comments. I think they are the same types of questions that we look at each other in the eyes every time we have a slightly modified product and try to go through the thought process of, you know, are we asking the right questions and do we really have the right focus on the issues and the questions associated with the product.

My only other comment, I guess, would be is that to remember that classification or reclassification is a process whereby -- and I can't even say it as well as I think Dr. Fearnot said it. I mean in terms of focusing on the risks and looking to see what controls we have associated with it.

This does not give away the fact -- depending on what a recommendation might be, does not give away pre-market control. FDA still retains pre-market control, certainly, in the Class II and in the Class III area.

If Class I is recommended, then I think we do lose some amount of control pre-market. Whether that is appropriate or not, I think, is an issue for each individual device. But I think the same people that would scrutinize a PMA are going to be the same people that are going to scrutinize a 510(K).

So, you know, I don't think the particular piece of the process that the FDA is involved with necessarily has to change dramatically.

DR. LASKEY: To that point, then are the rigors of bench testing the same for Class III and Class II?

MR. DILLARD: In this particular case, I would have to say yes.

ACTING CHAIRPERSON TRACY: Mike.

DR. DOMANSKI: Well, I guess it's time to move to make a motion relative to this, Cindy, or is

it?

ACTING CHAIRPERSON TRACY: Actually, I think it's time to ask the two gentlemen to step back, and then we will consider the questions that were put to the panel, I think.

MR. DILLARD: Just a point of clarification of the process. I would suggest we ask them for any other final comments they might have perhaps before we excuse them.

DR. FEARNOT: No comment.

ACTING CHAIRPERSON TRACY: Thank you. Okay, we are going to start first with the questions that were originally asked of the panel. I think you all have that in your blue packet, and in addition to inside the white binder.

The first question was: Does the proposed classification description sufficiently describe the percutaneous transluminal coronary angioplasty catheter?

The proposed device description -- do you have that there to stick up. The discussion that we have had here today -- there's just a couple of points

that I think we need to talk about briefly here.

As it is stated now, "A balloon catheter has a single or double lumen shaft with a balloon near the distal tip," which I think everybody is in agreement with that sentence. The catheter -- You might want to argue with that, but anyway.

"The catheter typically features a minimally compliant balloon constructed from a high density polymer." Are we going to ask for some change in the language there, and does anybody have a specific change in language on that?

DR. KRUCOFF: Cindy, I just have a question maybe to FDA -- what words like typically imply. Is there an implication?

MR. DILLARD: Briefly, the only clarification we have for real fuzzy language is probably in "reasonable assurance of safety and effectiveness." We kind of understand what that means. Beyond that, any fuzzy language that would be in this definition, I think, is open to interpretation.

So I think it would -- if you think it

needs to be tightened up, I think we all could certainly benefit from some suggestion.

ACTING CHAIRPERSON TRACY: I guess the specific two phrases then that were in question were "minimally compliant balloon" and "high density polymer."

DR. LI: Steve Li. I'm not quite sure I know enough about the engineering specifics to give the exact complete phrase, but I would suggest something like "the catheter typically features a balloon constructed from a polymer that has the following properties, pressure/diameter properties," and provide a range that would give you some latitude for future development but clearly keeps you out of the range you want to exclude.

DR. DOMANSKI: Or just say "has known pressure/diameter relationships."

DR. LI: But the urologic catheters are known. He just doesn't want that compliance.

DR. DOMANSKI: Yes, but I guess, see, your logic hazards would be unlikely to be used in the coronaries.

DR. LI: But that's the whole idea of the sentence, though. Exclude the material, though. See, he's using the mechanical property to describe the material, which is my problem. Normally, the material is chosen to match the mechanical property. It's a subtle but a very important difference if you are designing something.

DR. DOMANSKI: I hate to confine them to a series of numbers. I don't know, Jim, what do you think?

MR. DILLARD: In my usual fashion, I'll give you both options, which is the more open it is, I think, the way it is currently written, the more subject to FDA interpretation you are giving us or at least by way of a recommendation saying that, you know, FDA understands how to define those or interpret those fuzzy language, and that in the context of 510(K) the way we would interpret that language would be to compare it to other products of the known type by way of the structural characteristics and material kinds of properties. That's how we would interpret that, and that's the comparison we would draw.

If you think it's more important to be specific because we don't want technology or you don't believe that technology should creep any further than it currently is, then the more and more specific you get, the more tied in we are to what we currently know.

DR. DOMANSKI: Given the expertise -- Just talking to Dr. Li. Given the expertise inside the FDA for this, I would feel pretty comfortable with a somewhat looser language so that we don't tie their hands.

DR. LI: Well, I have no problem with that. I just don't like that particular loose language. In other words, if they said constructed form a polymer, I would be much more happy than in saying high density polymer, for instance. That phrase is very specific.

DR. DOMANSKI: Well, yes, the term "high density" may be vague. I think there are a couple of vague things in there. "Minimally" is vague, I think, and so perhaps is "high density."

DR. LI: Yes. Exactly. I'm not trying to

tie anybody's hands or limit anybody. I just want-- If you are going to use words, I would prefer them to have their appropriate technical meaning, is all I'm headed for.

ACTING CHAIRPERSON TRACY: Is there something going to be lost if we just say "a balloon constructed from a polymer"? That kind of leaves it a wide open field. I think that, as vague as this is, there is some constraints put on, and I think the FDA has a good understanding from the 820 other catheters that are already out there of what exactly that means.

So I'm not sure that it is, in my mind, important to change the language too much here, because you can, I would think, run into the problem of I have no clue what this means, but if you change the density by whatever measure, whether you are going to restrict something that really isn't substantively different.

DR. LI: Well, Steve Li again. I guess maybe I'm the only one in the room that's sensitive to this. But high density to a polymer person has a very specific meaning. Right? And .01 grams per cc.

change in density moves you from high density to low density.

So for a materials person, it's a highly specific term used, in this case, meant to be a general description, and that's my problem.

ACTING CHAIRPERSON TRACY: Is there that much variation within the catheters, the 820 catheters? Is there a difference between high and low density polymer catheters by the definition that Dr. Li is suggesting?

MR. DILLARD: Jim Dillard. I'll answer that question specifically and just say that, yes -- and one of my technical people are going to tell me exactly what that difference is here in a second. But, yes, there is a difference, and it certainly has to do with not only the different kinds of material, because we are talking about high density polymer here -- so there are some material concerns -- as well as it has a large impact on the strength of the overall catheter. I think those are important concepts to bring into this.

Let me say something generally as to why

this is important, because perhaps not everybody recognizes that the device description that you are helping us with right here, along with one of the other questions we have, which is the intended use, are the two things that really define what a product is, and that is written into the Code of Federal Regulations.

So if this product is reclassified, this particular description or, you know, something that is reasonably worked out, along with the intended use and the indications for use really define the product area.

So that's why it's important to have something here that people are going to understand.

ACTING CHAIRPERSON TRACY: Do I understand you correctly, that there are high and low density polymers that are currently within the approved devices. So that this statement then is really erroneous for what we have in place?

MR. DILLARD: Let me just maybe say real directly, it's not that important to say whether it's high density or not in this particular context.

DR. LI: But, importantly, though, if you say high density -- If I'm reading this and I'm going to develop another balloon catheter, if I see that phrase, you have wiped about 50 percent of the available polymers for me to use in this device.

DR. DOMANSKI: Well, then why don't we just get rid of it?

DR. LI: I said I was perfectly happy to.

DR. DOMANSKI: It sounds like a very poor choice of terms, actually.

ACTING CHAIRPERSON TRACY: Just "polymer"?

DR. DOMANSKI: Yes.

DR. KRUCOFF: Is it appropriate in a definition to use precedent? I mean, could we say "comparable to the existing range of devices in the market" or I mean, can we use what's out there as part of a definition or what would come forward?

MR. DILLARD: Jim Dillard. I would just say that that's inferred, based on the types of products we are talking about.

DR. LI: I'd be happy if we just took out "high density" and just call it a polymer.

ACTING CHAIRPERSON TRACY: So if we just take out "high density," and it is inferred that it's compared to the other products out there, then I think that gets around that problem.

The only other issue then is "minimally compliant balloon."

DR. DOMANSKI: I'd sure like to get rid of "minimally."

ACTING CHAIRPERSON TRACY: Does anybody have any --

DR. DOMANSKI: You can get rid of "minimally compliant."

DR. LI: I just don't know what -- Does everybody but me understand -- besides the two of us, know what minimally means?

DR. KRUCOFF: This is knuckle dragging cardiologist terminology. This is widely used terminology in the interventional community, but unfortunately, probably has a lot of relevance to considering this versus another device, and probably is a complete abuse of any real scientific terminology. That's probably what we are wrestling

with here.

When we usually think of compliant, minimally compliant, noncompliant balloons, there are some balloons where, really, as you go up in pressure, the balloon does get significantly bigger, half a millimeter or so larger.

Those balloon materials tend to be more compressible. They fold up. They get smaller. They are easier to slide across a lesion, but you're stuck with them once you are there, or if you are trying to get a half-size larger, you may use them intentionally.

Noncompliant balloons which, as were shown elegantly before, actually, are complaint if you crank them up high enough, are the ones that, as you put more pressure to them, they grow less. So if you are trying to embed steel into a rock, that's the type of balloon you would tend to use.

Minimally compliant are the ones kind of in the middle where they are a little bit of this and a little bit of that. So I think what we have inherited here are the abusive jargon of common usage,

but I think on behalf of whoever wrote this, this is all common usage in the interventional community.

I think how to translate it into a best definition is a different question.

DR. DOMANSKI: I think -- I do a fair amount of intervention, too, and I think the language as it sits here is too vague. I think to use that term is -- that requires definition. I think you got to get rid of it.

Besides, you may not want to limit it to what Mitch is defining as minimally compliant anyway.

ACTING CHAIRPERSON TRACY: Is there a better way of saying it that you could suggest?

DR. DOMANSKI: Yes. I'm sorry, why don't you go ahead? I suggested getting rid of it.

DR. KRUCOFF: I would go back to the precedent, that it may be more than implied. Maybe we ought to just say outright that the materials in compliance of which will be reasonably comparable to what is broadly used. Then you cover all three categories, and you don't abuse scientific terminology.

DR. DOMANSKI: But isn't that inferred in a 510(K)?

MR. DILLARD: Jim Dillard. That would be what we would be making the comparison to, are those products that were used in support of this whole application, and that's what really defines this product category.

So that would be what we would logically compare to.

ACTING CHAIRPERSON TRACY: Okay. So I'm not sure where that -- I have a problem with a statement that just says the catheter features a balloon, like a Mickey Mouse balloon. I don't know what limits that puts on you at that point.

DR. CRITTENDEN: We need to qualify the word compliant. The catheter tip features a compliant balloon.

ACTING CHAIRPERSON TRACY: Well, complaint is different from "minimally compliant."

DR. DOMANSKI: How about "of reasonable compliance for the clinical application," and reasonable then comes back to FDA to interpret within

the --

ACTING CHAIRPERSON TRACY: A balloon of reasonable compliance?

DR. DOMANSKI: For the clinical application.

DR. KRUCOFF: Do you want to say appropriate instead of reasonable?

ACTING CHAIRPERSON TRACY: Of appropriate compliance for the clinical application, constructed of a polymer? Can you live with that?

DR. DOMANSKI: You're going to hate this, but I want to ask a question. Could you construct this -- I mean, I've never thought about this before, but things like this really bring the best out, I guess.

Could you construct a balloon out of something other than a polymer?

DR. KRUCOFF: Yes, but not for a 510(K).

ACTING CHAIRPERSON TRACY: I would think then you would be --

DR. DOMANSKI: But not for a 510(K). Okay, that's fair. Cool. Okay.

DR. KRUCOFF: Now is nylon a polymer?

DR. LI: Yes. But there are like 30 different kinds of nylons.

DR. DOMANSKI: And define nylon.

ACTING CHAIRPERSON TRACY: Okay. "The balloon is designed to uniformly expand to a" -- I'm sorry, Renee?

DR. HARTZ: The first sentence is what bothers. You're going on through the rest of it. The first sentence bothers me the most, because the first sentence does not clarify whether we are talking about both on and over-the-wire catheters.

You're talking about the balloon itself, but are we talking about both uses, both types of catheters here?

MR. DILLARD: Jim Dillard. I believe that is what is talked about, certainly in the petition. So whether or not it needs to be more specific than that, that's certainly what our consideration would be, yes.

DR. HARTZ: This says "near the tip." See, words like "near" -- typically, generally, I

agree.

MR. DOMANSKI: Well, of course, I was going to suggest adding a sentence. At the end of this, I was going to suggest the sentence that I suggested for the beginning, which is suggested by -- Somewhere the FDA folks, I think, suggested a sentence that I want to add to the beginning later.

One can include "on or over-the-wire," but in the entire -- I guess, in fairness, in the entire universe that's all there is, really. It's the rapid exchange. It's on-the-wire and over-the-wire. So there are three different possibilities.

I guess the question is need one really specify that, if those are the only ones? I don't know the answer to that, but that's the question. I mean, do you really need that language?

ACTING CHAIRPERSON TRACY: I think, if that's the universe, then that's what you're looking to reclassify.

DR. DOMANSKI: On, over or rapid exchange.

MR. DILLARD: Jim Dillard. There is sort of a level of specificity here, which I think you are

grappling with, which is do you need to necessarily define what the world is today so that we are comfortable with that in the reclassification or do you have to really think beyond today to where the technology may evolve and whether or not it will actually then become part of this or would be excluded, which I think is a lot of what panels struggle with, with reclassification.

So I always advocate in those cases where, if you think it is important because the data right now currently supports two or three on-the-wire, over-the-wire type of designs that we currently have, that it is worthwhile having some of that descriptive language in the proposed device description, because it does give us then a framework from which to go from in terms of what it was we were talking about whenever we went for reclassification.

ACTING CHAIRPERSON TRACY: What was your sentence then, Mike?

DR. DOMANSKI: Well, the sentence that I thought ought to be added on the front end, which is really just a suggestion by the FDA, should then be

included. The way the sentence read without it -- and it needs to be added, I think -- is "PTCA catheters comprise angioplasty systems that operate on the principle of hydraulic pressurization applied through an inflatable balloon attached to the distal end."

Then perhaps to that sentence one could add, you know, that this -- or a second sentence that just says "This includes on-the-wire and over-the-wire systems, including rapid exchange devices."

ACTING CHAIRPERSON TRACY: Is that acceptable to the panel?

DR. DOMANSKI: That would be at the front of this thing or that would be one place to put it, would be just at the front, and then "A PTCA balloon catheter has a single or double lumen shaft near the distal tip." You know, you would change the -- You get rid of that phrase, because you have already said it once. But that would be the first sentence.

The second sentence would be: "A PTCA balloon catheter has a single or double lumen shaft," period.

ACTING CHAIRPERSON TRACY: Okay. That

seems acceptable to everybody then.

All right. We were at the point of "The balloon is designed to uniformly expand to a specified diameter and length at a specific pressure as labeled, with acceptable rates of inflation and deflation and acceptable burst pressure."

There were some comments about the word acceptable.

DR. DOMANSKI: I said specified instead of acceptable, because acceptable is vague. Well characterized.

ACTING CHAIRPERSON TRACY: Well characterized or defined instead of acceptable? Okay.

"The device generally features a type of radiographic marker to facilitate fluoroscopic visualization of the balloon during use."

DR. HARTZ: Are there any that do not have a radiographic marker?

MR. DILLARD: Jim Dillard. Not to the best of our knowledge.

DR. DOMANSKI: I guess the question is how wedded -- I mean, it would be idiotic. It seems to

have one without a radiographic marker. On the other hand, could for some reason somebody want one without it? I mean, that doesn't strike me as a large --

DR. SIMMONS: Certainly, no, with all the non-fluoroscopic stuff we are doing in EP, you know, with magnetic fields, echo fields, you may end up at some point in time doing your procedures without a lot of your --

DR. DOMANSKI: Yes, but I guess --

DR. KRUCOFF: Not as a 510(K).

DR. SIMMONS: Not as a 510(K). Right.

DR. DOMANSKI: Well, let's just pause briefly on that. Can we ask the industry folks if they have any thought about that? You know, it would be interesting to know. Do you want to be wedded to radiographic markers in your 510(K)s? They've all got them, but do you want to be wedded to it?

ACTING CHAIRPERSON TRACY: Could you use the microphone, please?

DR. FEARNOT: Fearnot. I think it's a small point at this juncture. I think MRIs might change that a bit. I think, as far as the device

itself, though, the marker or not having a marker is really a small part of the function of the balloon -- or the device in use.

Clearly, they all have markers today, because they are all placed with angiographic.

DR. DOMANSKI: Do you see -- You know, the reason I say this is because I'm told that we have now at NIH hired a guy who is going to do interventional MRI. Now I hasten to add that I'm not sure what that means, but certainly, in the context -- If he is going to be using balloons, it can't be with the kind of radiographic markers you are using, I would think.

DR. FEARNOT: You're probably correct.

DR. DOMANSKI: But it doesn't alter your balloon or the safety or efficacy of it to pull that radiographic marker. So maybe that shouldn't be in there.

DR. FEARNOT: I think what we know as far as characterizing the performance of the balloon and its pressures and the main issues of compliance and burst pressure and those things that have caused the complications, I know of no complications or risks

associated with the marker of any kind.

So I think that may be a real small point. You know, you may not want it in the definition.

DR. LASKEY: I think it's fair to say, if it doesn't have a marker, it's not going to be used in clinical practice.

DR. FEARNOT: I think it's irrelevant as to the device.

ACTING CHAIRPERSON TRACY: So it probably stays where it is then. Okay.

Is it important -- Again, this is the universe that we are talking about. So we do not need to specify that this does not include devices that are used for other deliveries, for delivery of medications, etcetera. Is that correct?

MR. DILLARD: Jim Dillard. I think that, in terms of when you actually go through the sheets and specifically talk about the devices and what they are and what they aren't, I think you can make a note of that during the particular process. But I think right now that is not what the petitioner is asking for, number one; and number two, that isn't generally

how we would interpret it either.

Just by way of a real quick point, the fact of the way it is worded there at the bottom -- "The device generally features a type of radiographic marker" -- that doesn't exclude the possibility of submitting an application without one proving why it still is reasonable.

So I don't think that particular language ties our hands, just as a point of reference.

ACTING CHAIRPERSON TRACY: Okay. Anymore comments on question number one then?

DR. CRITTENDEN: Do we need to limit the device's size or specify the size below which it is no longer 510(K)-able, if that's a verb?

DR. DOMANSKI: Well, PTCA says coronary angioplasty. So does that bracket it?

DR. CRITTENDEN: I suppose you can go further out into more distal vessels, if you thought that was appropriate, for smaller devices.

DR. DOMANSKI: I'm sorry. I'm missing it.

DR. HARTZ: That "C," we have to infer, is only coronaries?

ACTING CHAIRPERSON TRACY: Right. That's what that "C" means.

DR. HARTZ: Okay. See, a small iliac, you know --

MR. DILLARD: No. Jim Dillard. We are specifically talking about coronaries here.

DR. HARTZ: Okay.

ACTING CHAIRPERSON TRACY: Okay. If there is no more discussion on number one, we'll move to the second question, first part: "Have the health risks associated with PTCA catheters been adequately identified? If not, what are the additional risks that should be described?"

The list is up there for your viewing almost. I guess the -- trying to look through this list, there was some discussion that unstable angina is really not probably appropriate for this. It is more likely going to result in acute infarct. So there was a suggestion to remove the words "unstable angina" from this.

DR. KRUCOFF: Just for a point of discussion, somebody who has an angioplasty who

develops chest pain with ST depression while they are still in the hospital who goes back to the lab and has partial closure of the site, who is redilated is not an acute infarct.

That is a complication of the procedure. It obviously doesn't take in the whole world of unstable angina, but I do think there is a clinical outcome, if you will. Whether you call it recurrent ischemia, which is how it is usually characterized in the clinical trials, relative to this list, I think it's a significant incidence in reality as a result of the procedure.

ACTING CHAIRPERSON TRACY: As a result, not necessarily right within the lab experience but the night after.

DR. KRUCOFF: Right. And they go back to the cath lab the next day.

ACTING CHAIRPERSON TRACY: So does that seem reasonable, just to leave it in? There was another suggestion to list it separately, separate from acute MI as a separate complication. It seems as though, if there is a temporal difference, that might

be appropriate to separate it on a separate line.

There was a suggestion to add air embolization and infection, air embolization as another risk, infection as another risk. Any comments on those? Adam, keep them off? Adam?

There was a suggestion to be more specific, that we were talking about aneurysm formation within the coronary artery. I assume that's acceptable to everybody. And a suggestion to add that the vascular access site complications which may require surgery or surgical intervention -- is that acceptable to everybody to add that?

DR. LASKEY: Well, technically, those are not related to the PTCA catheter but to the guide catheter or the sheath. I mean, I don't know how Talmudic we want to be about this, but that is not related to the angioplasty catheter.

DR. KRUCOFF: Well, except, Warren, you know, if you are pulling back on your catheter and the balloon catheter is bulky and it sucks the guide catheter in -- I mean, again this is a very -- as you know, a very multi-factorial sort of potential to do

harm. I don't know why we would exclude it, actually.

MR. DILLARD: Jim Dillard. Just a point of clarification, that the fact of identifying all the potential risks associated with the procedure, I think, is important here, so that we can take a look at making sure that those risks of the procedure with a balloon catheter as well as the other accessory products are adequately looked at in terms of what the overall risks could be to the patient.

So I think it is important to at least put those on the table. We will look at them and see what ends up in sort of the final proposal, but I think it is important to certainly discuss them here.

ACTING CHAIRPERSON TRACY: So I think then that means that we would leave things like the coagulopathy, stroke in place in this list of risks, since it is attendant to the procedure in which the balloon is being used.

Were there any other discussion points on this?

DR. SIMMONS: Somebody had mentioned

during the presentation retroperitoneal bleeding. I guess you could say that is partly under vascular access site complications, but it's a significant complication.

DR. HARTZ: I agree with that, and I wonder if we should list this differently, say "emergency surgery for" and then list access site complications, retroperitoneal bleeding, guide wire complications, impending myocardial infarction. You could just list them that way.

ACTING CHAIRPERSON TRACY: Dr. Li?

DR. LI: Yes. Steve Li.

DR. HARTZ: Because it's not just emergency bypass surgery we are talking about. We're talking about various types of emergency surgery.

ACTING CHAIRPERSON TRACY: Dr. Li?

DR. LI: Just a -- This might be a stupid question. This is my nonfamiliarity with the area, but I see several references to two separate categories, balloon rupture and balloon burst.

Is there actually a difference between those two?

ACTING CHAIRPERSON TRACY: No.

DR. LI: Okay, fine. I didn't think there was, but it's listed separately several times through here.

DR. KRUCOFF: There's high density rupture.

ACTING CHAIRPERSON TRACY: Polymer rupture.

DR. LI: Those being minimal ruptures?

The other question I had: There's also references to other parts of the device having failures besides the balloon. I don't see anything other than the guide wire fracture, but there are references to other -- like device breakage, I guess, is the general category that are in there.

Is that something that we should put up on that list as well, because the only thing I know that is mechanical is the balloon rupture or burst.

DR. KRUCOFF: Krucoff. I actually think, Stephen, that's a great point, because just as an almost trivial sounding example, a very common factor of discussion of the operators of the device, a very

common event with array of balloons is when you prep the balloon, you aspirate the balloon lumen with a syringe to let capillary filling of the contrast material replace the air that's in the balloon when you take it out of the package.

In a novice's hands, they will frequently do that, leaning the end of the balloon connector on the table. And depending on whether you have already put the guide wire through the balloon or not or depending on what that balloon is made of, if to save space and make this a smaller balloon the channel for contrast flow is a relatively thin walled channel, what the fellow or novice will actually do is crimp the channel for the balloon, and you won't know that until you have the balloon across and try and inflate it.

So there are other kinds of mechanical failures, and this does get into this sort of thorny scenario. Is it the operator? Is it the balloon? Do we even know these things happen? I don't know how you list all that.

DR. LI: My question wasn't quite that

knowledgeable.

DR. KRUCOFF: Well, but this is a breakage. It's not the balloon, the rupture. It's down at the hub within the contrast channel that ultimately causes the device to fail, but it's not on this list. That's one of many.

ACTING CHAIRPERSON TRACY: I would think, though, that that's the type of information that is in labeling and physician training. I don't know that we would necessarily need to put it as a risk of the procedure.

DR. LI: Actually, I raised it because it shows up on some of the tables for things that happen to these devices. There was a category for device breakage that was separate from balloon burst.

ACTING CHAIRPERSON TRACY: It could be added as then a phrase, "other device malfunctions"?

DR. HARTZ: The noncompliant operator is risking that himself.

ACTING CHAIRPERSON TRACY: Okay. So yes then, add some phrase indicating other component device failure.

DR. LI: I guess on one of the tables it says, out of the 3,316 adverse events, 87 serious injuries were related to device breakage, whatever that means.

DR. DOMANSKI: And MAUDE reports some of these device failures.

DR. LI: Well, I just wasn't quite sure what device breakage meant, but if everybody understands what that means, it seems like that should be on the list. Okay?

ACTING CHAIRPERSON TRACY: So "other component device failures." Mr. Dacey, did you have a comment?

MR. DACEY: Are you through with that one?

ACTING CHAIRPERSON TRACY: Yes.

MR. DACEY: Okay. This is from my own personal experience. Maybe you can just help me with it a little bit.

Another reaction to contrast agent: Are we talking about life threatening or just a period of time of discomfort, because I experienced some extreme discomfort as a reaction to contrast agent, and I've

known of cases where people were put in life threatening. So does this require further clarification?

ACTING CHAIRPERSON TRACY: I think it runs the spectrum between discomfort to something that could be life threatening, but I think it probably just serves as a warning that that can pose a health risk to the patient.

DR. HARTZ: Is that covered under the original -- That particular complication is covered under the original consent to undergo coronary angiography. I mean, if there is any visualization whatsoever of the coronaries, it's not really relevant to this device. You have to visualize the coronaries through the angioplasty. So it's an unrelated --

ACTING CHAIRPERSON TRACY: Except that, as soon as you -- In many centers, as soon as you put a catheter in the coronary, you are going to anti-coagulate, which is not a piece of the angioplasty. So you are talking -- Again it's not, I don't think, right to dissect out the risks of any part of the procedure the patient undergoes versus the entire trip